



EUROPEAN COMMISSION  
DIRECTORATE-GENERAL FOR HEALTH  
AND FOOD SAFETY



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

## **Questions and Answers related to the United Kingdom's withdrawal from the European Union with regard to the medicinal products for human and veterinary use within the framework of the Centralised Procedure**

On 2 May 2017, the European Commission and EMA published a [Notice to marketing authorisation holders of centrally authorised medicines products for human and veterinary use](#), stating: "*The United Kingdom submitted on 29 March 2017 the notification of its intention to withdraw from the Union pursuant to Article 50 of the Treaty on European Union. This means that unless the withdrawal agreement establishes another date or the period is extended by the European Council in accordance with Article 50(3) of the Treaty on European Union, all Union primary and secondary law ceases to apply to the United Kingdom from 30 March 2019, 00:00h (CET). The United Kingdom will then become a 'third country'.*"

In this regard, marketing authorisation holders of centrally authorised medicinal products for human and veterinary use are reminded of certain legal consequences that need to be considered in a timely manner. Preparing for the consequences of the UK's withdrawal from the Union is not just a matter for European and national administrations, but also for private parties.

This first list of Questions and Answers (Q&As) has been drafted jointly by the European Commission and EMA and concerns information related to **establishment requirements** within the Union (EEA). The Q&As will be further updated and complemented in the near future.

### **1. What if I am a marketing authorisation holder established in the UK ?**

According to Article 2 of Regulation (EC) No 726/2004 the marketing authorisation holder must be established in the Union. Through the EEA Agreement this is extended to include also Norway, Iceland and Liechtenstein.

For centrally authorised medicinal products the marketing authorisation holder will therefore normally need to transfer its marketing authorisation to a holder established in the Union (EEA) (see Commission Regulation (EC) 2141/96 and [EMA Q&A on transfer](#)). This means that the addressee of the marketing authorisation decision changes to the new addressee.

### **2. What if I am an orphan designation holder established in the UK? (for medicines for human use)**

According to Article 2 of Regulation (EC) No 141/2000 the sponsor of an orphan medicinal product designation must be established in the Union (EEA).

For designated orphan medicinal products the holder will therefore need to transfer its designation to a holder established in the Union (EEA) (see [Checklist for sponsors applying for the transfer of Orphan Medicinal Product \(OMP\) designation](#) and the corresponding template) or it will need to change its place of establishment to a Member State of the Union (or EEA) and submit the corresponding documentation through a change of name and/or address of the orphan designation holder procedure provided the legal entity remains the same (see Guideline on the format and content of applications for designation as orphan medicinal products and on the transfer of designations from one sponsor to another, 27.03.2014).

### **3. What if I am a UK company with a MUMS (Minor Use Minor Species/limited market) status for my product? (for veterinary medicines)**

If the sponsor/applicant is established in the UK, the MUMS incentives would no longer be applicable with effect from the date of the UK's withdrawal from the Union, as a sponsor/applicant established within a third country cannot seek and receive MUMS/limited market classification in the Union (EEA). However, MUMS/limited market classification is connected to the product/indication and therefore transferable together with the product.

To formally acknowledge the transfer, the EMA requires a letter from the original sponsor/applicant officially informing the EMA of the transfer of the classification product and the MUMS/limited market classification from the original sponsor/applicant to a sponsor/ applicant established in the Union (EEA). This letter should state the MUMS outcome letter document reference number.

For already authorised MUMS/limited market veterinary medicinal products it is important to note that a transfer of marketing authorisation does not include a transfer of an MUMS/limited designation as this is subject to a different procedure. Therefore, for those authorised MUMS/limited market veterinary medicinal products the marketing authorisation holder needs to transfer the marketing authorisation (see: "What if I am a marketing authorisation holder established in the UK (H + V)?") and separately the MUMS/ limited market classification (see above).

### **4. What if my Qualified Person for Pharmacovigilance (QPPV) resides and carries out his/her tasks in the UK?**

According to Article 8 of Directive 2001/83/EC and Article 74 of Directive 2001/82/EC, the qualified person responsible for pharmacovigilance must reside and carry out his/her tasks in the Member State of the Union (EEA). The QPPV will therefore need to change his/her place of residence and carry out his/her tasks in the Union (EEA) or a new QPPV residing and carrying out his/her tasks in the Union (EEA) will need to be appointed. Changes in the QPPV, including contact details (telephone, and fax numbers, postal address and email address) may, for medicinal products for human use, be updated through the Article 57 database only (without the need for a variation) (see Variation Guideline C.I.8). Regarding medicinal products for veterinary use the changes should be updated through a variation (see Variation Guideline C.I.9).

### **5. What if my Pharmacovigilance System Master File is located in the UK (PSMF)? (for medicines for human use)**

According to Commission Implementing Regulation (EU) No 520/2012, the PSMF must be located within the Union (EEA). The supervisory authority for pharmacovigilance is the competent authority of the Member State in which the pharmacovigilance system master file is located. The marketing authorisation holder will therefore need to change the location of the PSMF to a Member State within the Union (EEA). Changes to the location of the PSMF (street, city, postcode, country) may be updated through the Article 57 database only (without the need for a variation) (see Variation Guideline C.I.8).

## 6. What if my manufacturing site of the active substance is located in the UK?

As of the date of the withdrawal of the UK from the Union, active substances manufactured in the UK will be considered imported active substances.

Directive 2001/83/EC and Directive 2001/82/EC state that manufacturing authorisation holders are obliged to use, as starting materials, only active substances that have been manufactured in accordance with the detailed guidelines on GMP for starting materials.

In addition, pursuant to Article 46b(2) of Directive 2001/83/EC, active substances for medicinal products for human use shall only be imported in the Union (EEA) if, inter alia, the active substances are accompanied by a written confirmation from the competent authority of the exporting third country which, as regards the plant manufacturing the exported active substance, confirms that the standards of good manufacturing practice and control of the plant are equivalent to those in the Union (EEA).

## 7. What if my manufacturing site of the finished product is located in the UK?

As of the date of the withdrawal of the UK from the Union, medicinal products manufactured in the UK will be considered imported medicinal products.

The competent authorities of the Union (EEA) shall ensure that the **import** of medicinal products into their territory is subject to an authorisation in accordance with Article 40(3) of Directive 2001/83/EC and Article 44(3) Of Directive 2001/82/EC. The authorisation is granted when a number of conditions, as defined in Articles 41 and 42 of Directive 2001/83/EC and Articles 45 and 46 of Directive 2001/82/EC, are fulfilled (e.g. availability of a qualified person within the Union (EEA), GMP inspection).

For centrally authorised medicinal products the marketing authorisation holder will therefore need to specify an authorised importer established in the Union (EEA) and submit the corresponding variation (see Variation Guideline B.II.b.2).

In addition, in accordance with Article 51(1)(b) of Directive 2001/83 and Article 55(1)(b) of Directive 2001/82 the marketing authorisation holder will need to specify a site of **batch control** in the Union (EEA) where each production batch can undergo upon importation a full qualitative analysis, a quantitative analysis of at least all the active substances and all the other tests or checks necessary to ensure the quality of medicinal products in accordance with the requirements of the marketing authorisation.

For centrally authorised medicinal products the marketing authorisation holder will need to change the location of its current UK based site of batch control to a location established in the Union (EEA) and submit the corresponding variation (see Variation Guideline B.II.b.2).

## 8. What if my batch release site is located in the UK?

In accordance with Article 51(1) of Directive 2001/83/EC and Article 55(1) of Directive 2001/82/EC, the qualified person of the manufacturing and importation authorisation holder is responsible to certify that each batch of medicinal product intended to be placed on the EEA market was manufactured in accordance with EU GMP requirements and the marketing authorisation.

For centrally authorised medicinal products the marketing authorisation holder will therefore need to transfer its current UK based site of **batch release** to a location established in the Union (EEA) and submit the corresponding variation (see Variation Guideline B.II.b.2).

**9. I am a UK based SME, would I still have access to financial and administrative assistance in accordance with Commission Regulation (EC) No 2049/2005 (the 'SME Regulation')?**

In order to be eligible for financial and administrative assistance, companies must be established in the Union (EEA) and meet the definition of an SME.

As of the date of the withdrawal of the UK from the Union, the guidance for non-EEA based companies shall apply also to UK based companies:

- to apply for SME status once the company has established a legal entity in the Union (EEA). For proof of establishment, the SME office requires a copy of the certificate of incorporation in the company's commercial register. In such cases, the SME declaration can be submitted in the name of the newly established subsidiary with details of the parent company to be declared.
- to indirectly benefit from the SME incentives through an Union (EEA) established SME regulatory consultancy. SME regulatory consultancies may seek to benefit from the provisions of the SME Regulation on behalf of non-EEA based clients, only if both they and the client meet the SME criteria (i.e. fall below headcount and financial thresholds). In this case, both the regulatory consultancy and the non-EEA based company should submit SME declarations. If successful, the regulatory consultancy would receive an SME notification and the non-EEA based company would be listed in an annex to that notification as an SME client company. It is not possible for an SME regulatory consultancy to be considered eligible if they are acting on behalf of non-SME clients, as this would be contrary to the objectives of the SME Regulation.

Further information is available on the EMA website ([link](#)) and in the SME User Guide ([link](#)).

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